TARGETS FOR DRUG DEVELOPMENT IN HIV NEUROPATHY

A.S.C. Rice*
Pain Research, Imperial College, London, United Kingdom

Summary: There are globally ~34 million people infected with HIV. About 40% of those people living with HIV, whose infection is suppressed by antiretroviral therapy (ART) and are often otherwise well, have a length-dependent distal symmetrical sensory polyneuropathy, which in most cases is associated with neuropathic pain. This makes sensory neuropathy 1 of the most prevalent clinical manifestations of HIV in the current era of combined ART and therefore an increasingly major area of therapeutic need. Sensory neuropathy is usually attributable to either viral–neuronal interactions and/or ART neurotoxicity.

Data will be reviewed for:

- the epidemiologic and risk factors of HIV-associated neuropathy
- efficacy of current therapies: a meta-analysis of current randomized controlled trials for neuropathic pain in HIV
- sensory profiles and other clinical characteristics in HIV-positive patients with and without sensory neuropathy
- laboratory animal modeling of HIV GP120-induced neuropathy, including ethologically relevant complex pain behaviors and pharmacologic analysis
- laboratory animal modeling of ART neurotoxicity, including ethologically relevant complex pain behaviors and pharmacologic analysis
- use of gene microarray studies of animals models to reveal novel drug targets

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UPDATE ON THE STATUS OF ARTEMISININ RESISTANCE

P. Ringwald*
World Health Organization, Geneva, Switzerland

Summary: Drug Resistance and Containment Unit, Global Malaria Programme, World Health Organization, Geneva, Switzerland.

Global malaria control has been threatened by resistance to antimalarial medicines. *P falciparum* resistance to chloroquine and pyrimethamine both originated in Southeast Asia and subsequently spread to Africa with substantial implications for global public health. Similarly, in the 1980s, resistance to mefloquine emerged rapidly on the western border of Cambodia and on the northwest border of Thailand only a few years after its introduction. In April 2001, WHO recommended the use of artemisinin-based combination therapies (ACTs), combining an artemisinin derivative, known for its rapid action and short elimination from the body, with another drug characterized by a different mechanism of action and slow elimination.

Emerging *P falciparum* resistance to artemisinin derivatives is a major global public health concern. WHO first issued a warning about the threat of artemisinin resistance in the Greater Mekong subregion in 2005, after routine efficacy studies showed delayed clearance after ACTs. The first cases of confirmed artemisinin resistance were found in western Cambodia, along the Cambodia–Thailand border in late 2006. The 4 countries most affected by the emergence of artemisinin resistance are Cambodia, Myanmar, Thailand, and Vietnam. Despite observed changes in parasite sensitivity to artemisinins, ACTs continue to cure patients, provided the partner drug is efficacious. However, once resistance to artemisinin emerges, it is more likely that resistance to the partner drug will also develop and vice versa. Currently and in absence of a molecular marker, the best available indicator of suspected artemisinin resistance is the proportion of patients who are still parasitemic at day 3 (72 hours) after a full course of an ACT.

In 2010, WHO developed the Global Plan for Artemisinin Resistance Containment (GPARC). The plan was drafted after a consultation with all constituencies of the Roll Back Malaria Partnership, as well as a range of donor organizations and industry partners. WHO is also currently implementing an emergency response plan to scale-up efforts to contain artemisinin resistance in the Greater Mekong subregion. The presentation will provide an update of the current status of artemsinin resistance and containment activities.

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UNDERGRADUATE TRAINING FOR MEDICAL STUDENTS IN CPT AND PRESCRIBING

S. Ross*
Division of Medical and Dental Education, University of Aberdeen Aberdeen, Aberdeen, United Kingdom

Summary: Prescribing is a complex task and is often undertaken by the most inexperienced doctors. From day 1, new doctors need to be able to prescribe safely and rationally. It is clear that this requires more than traditional textbook knowledge of pharmacology. Preparing new graduates to be effective prescribers is 1 of the major concerns of modern undergraduate medical education. Evidence suggests that this training could be improved, although there is debate about the most effective methods for doing so.

This presentation will review the perceived deficiencies of current teaching, the challenges of delivering effective prescribing education, and the available evidence on a range of teaching and learning methods. In particular, the UK British Pharmacological Society 2012 recommendations for undergraduate education in clinical pharmacology and therapeutics will be used as an example of how medical educators might approach this difficult area.

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COMPLEXITY OF PREDICTING THE MAGNITUDE OF DRUG-DRUG INTERACTIONS IN AN INDIVIDUAL PATIENT: THIS CANNOT FIT TO A POCKET GUIDE; IPAD MAY BE!

A. Rostami-Hodjegan*
School of Pharmacy and Pharmaceutical Sciences, University of Manchester, Manchester, United Kingdom

Summary: The increased prominence of in vitro–in vivo extrapolation (IVIVE) capabilities has helped with recognizing the potential of drug–drug interactions (DDI) at early stages of drug discovery. Latest regulatory guidelines by the EMA and FDA provide recommendations for conduct of IVIVE through modeling. They are designed to protect the public from adverse effects associated with likely DDI by appropriate labeling or preventing the marketing of drugs with unmanageable DDI. However, DDI in an individual patient are determined by a myriad of variables. Prescribers may use labels in the clinical practice; nonetheless, currently, labels do not provide information for all the different permutation of conditions that put certain subgroup of patients at higher risk (eg, comorbid diseases, genetics, age and intake of several drugs). Some recent attempts by both the FDA and EMA have moved the focus from an average individual to a perceived susceptible patient (eg, chronic renal failure).

Creation of user-friendly interface computer programs of DDI prediction, which takes the sources of variability into account, may assist with the prediction and management of DDI in an individual patient. The required information on drugs (ie, affinity to various enzymes, nonenzymatic routes, permeability, protein binding, inhibi-